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MODULE 21

BLOOD BORNE PATHOGENS

Presenter: Capt. Mario E. Fajardo, M.D.
Occupational Medicine Physician
Human Factors Division (G-WKS-3)

Disclosure: Capt. Fajardo does not have any financial arrangements or affiliations with any corporate organizations that might constitute a conflict of interest with regard to this continuing education activity.

Goals:

1. Learn about blood Borne Pathogens.
2. Know the effects exposure to Blood Borne Pathogens.
3. Understand the major diagnostic steps.
4. Learn the surveillance principles of Blood Borne Pathogens.
5. Learn about prevention and "Universal precautions".

Note: This lecture material is a summary of information extracted from various sources dealing with this extensive subject matter. The presenter takes no authorship of this material. For more detailed information readers are referred to the following reference material:

1. OSHA Blood Borne Pathogen Standard 29 CFR 1910.1030 (http://www.osha-slc.gov.
2. Chapter 12 Medical Manual COMDTINST M6000.1B – Blood Borne Pathogen Protocol (Protocol #21).
3. US Naval Flight Surgeon's Manual: Third Edition 1991: Chapter5: Internal Medicine: Section 6: Infectious Disease.
4. Virtual Naval Hospital web site: http://www.vnh.org. Sections on Viral Disease; Screening for Human Immunodeficiency Viral Infections; and Hepatitis B.

Exposure Effects

Bloodborne pathogens are defined as any pathogenic microorganism present in the blood of humans, which are able to cause human diseases. The primary Bloodborne Pathogens (BBP's) include **Human Immune**

Deficiency Virus (HIV), Hepatitis B (HBV), and Hepatitis C (HCV). **HIV**, which was recognized as an infectious cause of an unusual immunodeficiency syndrome, is a retrovirus, which is transmitted, in a similar mode to that of hepatitis B virus. **HBV**, and **HCV** along with Hepatitis A Virus **(HAV)** are responsible for the vast majority of hepatitis cases worldwide. **HAV**, which is spread by the fecal-oral route, and is amenable to prophylactic measures is not considered a BBP and will not be discussed in further detail. **HBV**, also known as "serum" hepatitis, is less of a risk for endemic outbreaks than HAV but is also less amenable to prophylactic measures. **HCV,** formerly Non A- Non B hepatitis, is responsible for most cases of post-transfusion hepatitis and presents a significant risk for the development of hepatocellular carcinoma.

BBP's can be transmitted directly through the skin by needle punctures and other sharp objects, by spilling body fluids or secretions over unprotected skin openings or mucus membranes (eyes, nose, mouth), through parenteral contact with blood or other potentially infectious materials, or by aerosols produced when opening a specimen receptacle, or by specimen centrifugation, or when specimens are splashed into eyes during handling and processing. It can also occur indirectly when the outside of containers, specimen vouchers, or waste products are contaminated. Potentially proven infectious materials include: blood, semen, vaginal secretions, breast milk and saliva. The risk of percutaneous transmission is 0.3% from HIV infected blood, 1.8% from HCV, and 3.0% from HBV. The most frequently affected individuals are health care workers (needle stick injuries), housekeepers, janitors, police, EMT's / firemen, and hazardous waste workers.

Since the potential for infectivity of patient's blood and body fluids is not routinely known, it is essential that all workers conform **to blood and body fluid precautions,** regardless of any lack of evidence of infectiousness-"universal precautions".

Required surveillance

Enrollment in OMSEP for BBP exposure is based on OSHA guidelines (29 CFR 1910. 1030). These guidelines apply to all workers who reasonably anticipate contact with BBP's as a result of the performance of their duties. Determination of exposure must be based on the definition of occupational exposure without regard to personal protective clothing and equipment. Careful review of job classifications within each particular work environment should be the final determining factor. Exposures should be listed according to:

1. Jobs in which all workers have occupational exposure (i.e. lab personnel) and,

2. Jobs where only some of the workers may be exposed (i.e. alien migrant operations). In these circumstances all the specific tasks and / or procedures potentially causing the exposure must be clearly listed.

Coast Guard health care workers, hazardous waste workers, EMT's / firemen and personnel involved in alien migrant operations (AMIO) are at potential risk for exposure to BBP's. Enrollment requirements are met by completing the Acute Exposure Information Form used to record any unexpected exposures and for verification of notification of the appropriate agencies.

Information to medical personnel

Acute viral hepatitis is a serious operational problem, which has significantly altered the course of many military operations. According to established classification acute hepatitis is a self-limited liver injury of <6 months duration and chronic hepatitis represents a hepatic inflammation >6 months. The usual course of acute viral hepatitis is six to 10 days of acute symptoms associated with a variable rise in ALT/AST and bilirubin. The common clinical presentation includes the symptom complex of anorexia, nausea, right upper quadrant pain and tenderness, hepatomegaly, and jaundice. In individuals with fulminant infections, the prothrombin time will increase which is a poor prognostic sign. While cases must be individualized, excessive convalescent leave is rarely indicated. If the clinical course is benign the patient's may return to" activities as tolerated" as soon as the appetite returns, even if complete normalcy of AST/ALT has not been achieved. However, adequate outpatient follow-up is mandatory.

Acute viral hepatitis has serological markers that enable the clinician to distinguish between the viral causes of virtually identical clinical presentations, helping to predict chronic sequelae and infectivity in **HBV** infections. Important serological markers to follow include: HB_sAg, HB_e Ag, HB_cAg, HB_sAb, HB_e AB and HB_cAb. The AST and ALT should also be evaluated at monthly intervals following their initial rise and decline. **HCV** hepatitis, to date, has no serological markers that have been exclusively associated with blood transfusions, making this a diagnosis of exclusion based on the appropriate clinical setting.

Specific Bloodborne Pathogens are discussed in further detail:

Hepatitis B

Serologic evidence precedes clinical symptoms by approximately 1 month. Hepatitis B is the leading cause of liver-related deaths from cirrhosis and hepatocellular carcinoma worldwide; is especially frequent in drug abusers, male homosexuals,

and chronic dialysis patients; 5% to 10% of adults in the US have had the disease; and 10% develop a chronic carrier state and constitute an infectious pool.

Diagnosis

Hepatitis B surface antigen (HBsAg) is found in acute illness and becomes positive 1 to 7 weeks before clinical disease. It remains positive 1 to 6 weeks after clinical disease and in chronic carrier states. Blood-containing HBsAg is considered potentially infectious.

Hepatitis B antibody (Anti-HBs) is an antibody against the surface antigen of hepatitis B and appears weeks to months after clinical illness. The presence of this antibody confers immunity and indicates prior disease (if hepatitis B core antibody positive) or vaccination (if hepatitis B core antibody negative).

Anticore antibody (Anti HBc) appears during the acute phase of the illness and its presence can be used to diagnose acute HBV infection especially in the “window period” when both HBsAg and HbsAb may be undetectable. Presence of HBcIgM denotes acute infection and IgG appears chronically. The latter may be protective against reinfection.

Hepatitis B e antigen (HBeAg) is a mark of infectivity both acutely and chronically.

NOTE: Those who are hepatitis B carriers or have chronic active hepatitis will be HBsAg positive.

Prophylaxis

Hepatitis B vaccine at time 0, 1 and 6 months given in the deltoid muscle. Hepatitis B immune globulin (0.05-0.07 ml/kg) should be given soon (preferably within 48 hours) after a sexual or needle Stick exposure along with concurrent vaccination.

Treatment

Lamivudine and famciclovir have been used to treat chronic hepatitis B; protocols are not well developed. Interferon alpha-2b is approved and is in more widespread usage.

The Serological Markers for HBV and their clinical significance are illustrated in the following tables:

Serological Markers for HBV and Their Sources	
Serological marker	Source/Significance
Hepatitis B surface antigen (HB_sAg)	Antigenic determinant found in the HBV viral coat; present during acute and chronic HBV infections.
Hepatitis core antigen (HB_cAg)	Antigenic component of double stranded DNA core; generally not directly detectable.
Hepatitis e Antigen (HB_eAg)	Released from core during viral replication; directly correlates with HB infectivity.
Hepatitis B surface antibody (HB_sAb)	Reflects immune response to HBV infection; directed against surface antigen.
HBV Core Antibody (HB_cAb)	Core antibody is an immune response to viral replication. An IgM cAb reflects acute infections while an IgG cAb reflects old or chronic infection.
Hepatitis B e Antibody (HB_eAb)	Antibody directed against e antigen, reflects decreasing viral replication and beginning of resolution of the infection.

Clinical Interpretation of Serological Markers for HBV						
Test						Interpretation
HB_sAg	HB_sAb	HB_eAg	HB_eAb	HB_cAg (total)	HB_cAg (IgM)	
+	-	-	-	-	-	Incubation or early acute HBV infection
+	-	+	-	-	-	Early acute HBV infection
+	-	+	-	+	+	Acute HBV infection
+	-	-	$\pm$	+	+	HBG_sAg "widow" of acute HBV infection
-	-	-	+	+	+	Convalescence
-	+	-	+	+	+	Early recovery (up to 8 months)
-	+	-	+	+	-	Recovery (after 8 months)
+	-	$\pm$	$\pm$	+	-	Chronic HBV carrier, chronic hepatitis

Hepatitis C

Accounts for 20% to 40% of acute hepatitis in the United States. Hepatitis C also causes 90% of post transfusion hepatitis. The virus has an extremely high mutation rate and is thus not easily neutralized by the body's antibody response. Acute infection is usually asymptomatic; with 20% of patients developing jaundice, and 75% of those infected developing chronic disease with chronically elevated ALT (2- to 8-fold normal), and 20% of patients eventually developing cirrhosis. This can take years to decades to occur. The degree of ALT elevation does not correlate with the severity of disease. The severity of disease can be evaluated only with a liver biopsy. Hepatitis C infection is a risk factor for the development of hepatocellular carcinoma.

Risk factors

Most patients with hepatitis C have a history of intravenous drug abuse. Other risk factors include history blood transfusion, tattoos, alcohol abuse and cocaine snorting. Epidemiological evidence suggests that it can be transmitted sexually with risk of transmission increasing with duration of a relationship but with a very low incidence (<5%).

Diagnosis

Serologic tests that probe for antibodies produced in response to several viral antigens are now available for the diagnosis of hepatitis C. These tests are highly sensitive and specific. If testing low risk populations, RIBA (recombinant immunoblot assay) test should be obtained since the ELISA has a higher false-positive rate.

Polymerase chain reaction (PCR) can detect minute quantities of HCV RNA present in blood as early as 1-2 weeks after infection. Qualitative PCR tests detect as few as 100 HCV RNA copies, and quantitative tests detect a lower limit of 500-2000 copies.

Genetic heterogeneity of HCV identifies at least 6 distinct genotypes (with numerous subtypes). Different genotypes have geographic and epidemiological differences, and they are good predictors of response to interferon.

Treatment

Aim is to eradicate the virus and halt progression of the disease.

Liver fibrosis can be reversed to some degree with treatment.

Who refer for treatment? Anti-HCV- positive patients with persistently elevated ALT levels, detectable HCV RNA, and a liver biopsy that indicates either portal or bridging fibrosis or at least moderate degrees of inflammation and necrosis. There is no benefit of treatment in patients with a normal ALT.

Screening of those with normal initial liver biopsy but elevated ALT. Patients with elevated ALT but a normal initial biopsy should have repeat biopsy every 3-5 years to determine progression and need for treatment. There is no need for screening biopsies in those with normal transaminases.

Therapy

The goal of therapy is to eradicate HCV RNA. Alpha- interferons can be useful in treating chronic hepatitis C but should be administered under the care of a hepatologist. The usual dose is 3 million units 3 times per week for 6 months. There is a less than 40% response rate, and multiple courses may be necessary to achieve normalization of ALT. There may be multiple side effects of therapy, including flu-like symptoms, anorexia, malaise, fatigue, myalgias, fever, myelosuppression, hair loss, thyroid dysfunction and depression.

Combination therapy with ribavirin and IFN alfa-2b is superior to IFN monotherapy is becoming the treatment of choice. Ribavirin is teratogenic, an abortifacient and can cause hemolytic anemia. Therefore, hemoglobin needs to be checked frequently and patients should use birth control measures for up to 6 months after completing therapy.

Future therapies include the use of IFN attached to polyethylene glycol ("pegylated IFN") that prolongs the drug's $t_{1/2}$ and delivers a higher amount of the drug.

Human Immunodeficiency Virus - (HIV)

Has been recognized as a major public health problem for men and women, with between 5 and 10 million persons infected worldwide.

Risk Factors

It can be acquired by homosexual or heterosexual through intimate contact, by receiving infected blood or blood products, or by inoculation via needles contaminated with infected blood (IV drug use, tattooing, etc). There is also good evidence that transmission via open skin wounds exposed to infected blood or saliva occurs, though such transmission is rare.

Pathogenesis

HIV infects predominantly T_4 (helper) lymphocytes and macrophages. These cells express the CD4 surface antigen to which the virus surface glycoproteins bind. Once bound, the virus inserts its RNA genome into the cell, which undergoes reverse transcription to viral DNA. This DNA is then incorporated in the host genetic material where it can either remain dormant, express new viral RNA to make new virus, or possibly serve as an oncogene.

The destruction of infected lymphocytes and other immune cells result in a state of immunodeficiency.

Diagnosis

Some patients experience a flu-like illness when initially infected, but often there are no symptoms. A very variable, prolonged period may pass in which there are no signs or symptoms as immunosuppression proceeds. When the immune system is sufficiently impaired, infections with various organisms usually not pathogenic occur. These so-called opportunistic infections include fungi (*Cryptococcus neoformans*, *Histoplasma capsulatum*, *Candida species*, etc.) viruses (*Herpes species*, *Cytomegalovirus*, *Varicella*, etc.), bacteria (*Mycobacterium tuberculosis*, *M. avium*, encapsulated organisms, etc.), and parasites (*Pneumocystis carinii*, *Giardia* species, *Toxoplasma gondii*, etc). The clinician should be attentive to signs of global dementia that occur in the absence of an opportunistic infection of the CNS. This appears to be a direct consequence of HIV viral infection and precedes any other clinical manifestation in between 10 and 25 percent of infected patients who develop AIDS. Initially, there are mild cognitive defects involving judgment and memory, which progress to a severe global dementia.

Treatment

No curative therapy exists at this time for HIV infection. Therapy is directed at treatment of complications, and some progress is being made in antiviral therapy.

Disposition

All seroconverters are permanently disqualified from all special duties. Screening of all applicants to military service is performed using enzyme linked immunosorbent assay (ELISA) to detect antibodies to the virus in patient serum. If positive, the test is repeated. A positive repeated test is confirmed using a Western blot technique for specific antibodies before a patient is identified as "HIV-positive". HIV positivity, thus defined, is disqualifying for enlistment and commissioning in the armed forces. Seroconversion while on active duty requires an inpatient evaluation at a major treatment facility for classification, according to the Walter Reed Staging System.

Table 5-13 Walter Reed Staging System

	WALTER REED/DOD STAGING SYSTEM						NAVY CATEGORY
	HIV Ab A/O VIRUS	CHRONIC ADNPTHY	T-HELPER CELLS	DHS	THRUSH	OI	
1	+	-	> 400	WNL	-	-	A
2	+	+	> 400	WNL	-	-	
3	+	+/-	< 400	WNL	-	-	B
4	+	+/-	< 400	P	-	-	INCLUDES ARC
5	+	+/-	< 400	P/C	a/o +/-	-	
6	+	+/-	< 400	P/C	+/-	+	C INCLUDES AIDS

KEY: DHS- delayed hypersensitivity testing, OI- opportunistic infection

Examination

Each examination should include as a minimum:

1. A detailed work history and medical history with particular attention to:

   Past and present history of exposures to BBP's.

   Smoking and alcohol use history.

   Any symptoms of skin irritation, bleeding or recurrent dermatitis.

   Any CNS symptoms, including headaches, nausea, vomiting, dizziness, weakness, and disorientation.

   A review of the immunologic and hematopoietic systems.

2. A system specific physical examination with attention to the skin, mucous membranes, respiratory, and nervous system including a mental status evaluation.

3. The following laboratory tests: CBC, and WBC counts with differential, CD4 counts, immunoglobulins, platelet counts, liver enzymes and hepatitis profile and a multichemistry panel (including glucose, BUN, total protein and creatinine) and urinalysis.

Specific requirements

In addition to general requirements the physician should address:

a. Any other medical conditions, which could place the worker at greater than normal risk.

b. The periodicity of the next evaluation and/or referral to the appropriate specialty clinic.

c. The recommended duty limitations, hygiene care and infectious disease precautions.

d. The exposure risk (unprotected exposure) for HIV, HBV and HCV.

e. The medical officer should obtain the following specific information:

f. Determine the SOURCE status for HIV, HBV and HCV.

g. Determine the baseline status of the EXPOSED to HIV, HBV, and HCV.

h. Determine the EXPOSED immune status for HBV.

i. Determine mode of transmission: percutaneous, mucous membranes, sexual, other.

j. Determine SOURCE status: HIVAb, HBsAg, HCVAb.

k. Determine EXPOSED status: baseline HIVAb, HBsAg, HCVAb, HBsAb, HBV immune status if vaccinated.

l. Determine HIV post exposure prophylaxis (MMWR 1998)

m. Determine exposure codes (EC); HIV status codes (HIV SC)- use CDC Algorithm.

n. Make post exposure evaluation: HIVAb, HBsAg, HCVAb, liver enzymes.

o. In addition the medical officer should establish safe practice rules:

“Universal Precautions”

Defined as an approach to infection control where all human blood and body fluids are treated as if known to be infectious for blood borne pathogens. Specimens that entail "universal precautions" are all excretions, secretions,

blood, body fluid, and any drainage. Personnel should protect themselves from contact with these specimens by using the appropriate barrier precautions to prevent cross-transmission and exposure of their skin and mucous membranes, especially the eyes, nose, and mouth.

- Gloves must be worn when handling any biologic specimen and when touching blood, body fluids, mucous membranes or non-intact skin of all patients. Disposable, nonsterile latex or vinyl gloves provide adequate barrier protection. Gloves should be worn during routine laboratory procedures as well as phlebotomy. Phlebotomists should always change gloves and properly dispose of them between patients. Hands should be washed for 15 seconds whenever gloves are changed.

- Protective clothing, such as laboratory coats, cloth gowns, aprons, etc., should be worn when there is a chance for spraying or splashing of blood and body fluids. If the protective clothing becomes visibly contaminated with blood or body fluids it should be changed immediately to prevent contamination of personal clothing or skin. Protective clothing should not be taken home for laundering. Protective clothing should also be removed whenever leaving the laboratory.

- Protective eyewear such as goggles, safety glasses with side protection, and facial shields MUST be worn if there is significant potential for the splattering of blood and body fluids to the eyes, nose or mouth. In most situations splash shields will suffice.

Other safe practice rules

Other "Universal Precautions" that should be followed in the proper operation of a clinical laboratory or physician's office laboratory are:

1. Never pipet by mouth and never blow out pipets that contain infectious material or other liquids.

2. Avoid using syringes whenever possible and dispose needles without recapping, bending, or cutting, in rigid puncture-resistant containers clearly marked as biohazardous.

3. Disinfect and decontaminate all work surfaces and devices where biologic materials are handled at completion of work. Sodium hypochlorite (0.5%) or some other proper disinfectant can be used. All spills should be immediately disinfected with 0.5% sodium hypochlorite. Contact should occur for at least 15 minutes.

4. No warning labels are to be used on patient specimens.

5. Properly dispose of contaminated laboratory supplies (biohazardous waste). All contaminated supplies may be incinerated or autoclaved prior to being discarded.

6.Obtain immediate treatment for accidental and inappropriate contact with biohazards, such as a needle stick. The incident should be reported to the supervisor so that appropriate prophylactic measures can be taken.

7.Strongly encourage frequent hand washing for 15 seconds in the laboratory. Employees must wash hands before leaving the laboratory.

PROCEED TO POST TEST